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Fluconazole versus Voriconazole: *Candida glabrata* biofilms response to different azoles

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Candida glabrata is the second most prevalent yeast in fungal infections, especially in immunocompromised and/or hospitalized patients. The azole resistance within this species is very well-known and results in a low therapeutic response of *C. glabrata* infections, particularly when associated with biofilms. So, the main goal of this work was to understand the different efficacies of two azoles against *C. glabrata* biofilms: fluconazole (Flu), a long time used drug, and voriconazole (Vcz), a recent drug used only in hospitals.

Antifungal (Flu and Vcz) susceptibilities were determined in preformed 24-h-biofilms of different strains of *C. glabrata* (clinical isolates and a reference strain). The *ERG* genes expression profiles of *C. glabrata* biofilms cells were determined. Additionally biofilms' matrices composition and the retention of the two azoles within the biofilm matrix were evaluated.

The results showed that *C. glabrata* biofilms are more susceptible to Vcz than Flu. Quantitative Real-Time-PCR results revealed an overexpression of the three *ERG* genes in the presence of both azoles. However, the *ERG* expression was more dependent on the strain than on the agent. The matrix content was analyzed following biofilm exposure to antifungal agents and it was noticed a decrease in proteins, an increase in carbohydrates (also β 1,3-glucans) and ergosterol was also found. A further evaluation was made with the determination of the concentration of the agents diffusing through the biofilm, which showed a remarkable difference between the two drugs, with Vcz reaching more the cells than Flu, which could explain the differences in biofilms susceptibilities.

To conclude, this study showed that the better performance of Vcz in *C. glabrata* biofilms maybe due to its smaller molecule and therefore to its better absorption within the biofilm.